IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) [redacted]
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC. Plaintiff/Counter-Defendants.	REDACTED - PUBLIC VERSION

SAREPTA THERAPEUTICS, INC. AND THE UNIVERSITY OF WESTERN AUSTRALIA'S OPENING BRIEF IN SUPPORT OF THEIR MOTIONS TO EXCLUDE EXPERT OPINION AND TESTIMONY

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TABLE OF ABBREVIATIONS

Abbreviation	Description
'851 Patent	U.S. Patent No. 9,994,851
Sarepta	Defendant/Counter-Plaintiff Sarepta Therapeutics, Inc.
UWA	Counter-Plaintiff The University of Western Australia
NS	Plaintiff/Counter-Defendants Nippon Shinyaku Co., Ltd. and NS Pharma, Inc.
Patent Office	United States Patent and Trademark Office
ASO	Antisense Oligonucleotide
POSA	Person of Ordinary Skill in the Art
Asserted Claim	Claim 1 of U.S. Patent No. 9,994,851
Ex. ___	Exhibit ___[1]
Bold and Italic	Emphasis added unless indicated otherwise

[1] Refers to Exhibits to the accompanying Declaration of Megan E. Dellinger in Support of Sarepta Therapeutics, Inc. and The University of Western Australia's Motions to Exclude Certain Opinions and Testimony of Plaintiff/Counter-Defendants' Experts.

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I. INTRODUCTION

Prior to the May 6, 2024 pretrial conference, NS's invalidity arguments centered on its position that only a small subset of the claimed ASOs were required to be 100% complementary to the target "Exon 53" sequence, allowing the claims to cover ASOs with random and haphazard sequences. The Court gutted those arguments when it revisited Judge Williams's prior claim construction, and held that the entire sequence needs to be complementary. Unprepared for trial on that substantially-narrower construction, NS went back to the cutting room floor, reviving previously-abandoned or rejected arguments, and issuing new expert reports from both of its technical experts, Drs. Hastings and Wood.

Both reports are riddled with unreliable, misleading, and/or erroneous positions that have no business being in front of the jury. For example, Drs. Hastings and Wood espouse and rely on a specialized claim construction of "morpholino" that departs from the plain and ordinary meaning that they and NS previously used. And Dr. Wood testifies on ***inventorship***—which is not even an issue in the jury trial—by offering his subjective opinion on whether the '851 Patent's inventors "recognized and appreciated" the claimed invention.

This and other opinions and testimony from Drs. Hastings and Wood run afoul of Federal Rule of Evidence 702 and should be excluded.

II. NATURE AND STAGE OF THE PROCEEDINGS

NS sued Sarepta on July 13, 2021, asserting that Sarepta infringes claims of seven U.S. patents. D.I. 2, 86. NS also asserted declaratory judgment claims that three UWA patents, including U.S. Patent No. 9,994,851, are invalid. *Id.* Sarepta and UWA counterclaimed, alleging NS infringes their patents and that NS's patents are invalid. *See* D.I. 89, 328. The only Sarepta/UWA patent remaining in this case is the '851 Patent.

Before the scheduled May 2024 trial, NS asserted invalidity of the '851 Patent under

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35 U.S.C. § 112, arguing that the claim construction for "base sequence" was very broad because it included ASOs with as few as 12 bases that are complementary to the target sequence in exon 53. *See* D.I. 399-401. Following the pretrial conference, the Court clarified that claim construction, significantly narrowing it to ASOs with base sequences that are "100% complementar[]y to consecutive bases of a target region of exon 53 throughout the entire length of the [ASO]." D.I. 573. NS then advised the Court that it "is not in a position to proceed to trial" and requested additional expert discovery to address the claim construction. D.I. 569 at 3. On July 2, 2024, the Court issued an amended scheduling order, providing for supplemental technical expert discovery "related to issues . . . that are implicated by the Court's clarified and/or amended claim construction[.]" D.I. 597 at 2. The parties have completed supplemental expert discovery. Trial is now scheduled to start with jury selection on December 13, 2024. D.I. 597 at 3.

III. LEGAL STANDARD FOR ADMISSIBILITY OF EXPERT OPINIONS AND TESTIMONY

Experts may only proffer opinions and testimony if their "scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue." FED. R. EVID. 702(a). As emphasized in revised Rule 702 (effective Dec. 1, 2023), the proponent of an expert's opinions and testimony bears the burden to demonstrate that it is "more likely than not" that this expertise is helpful, *id.*, that the expert's "testimony is based on sufficient facts or data" and "is the product of reliable principles and methods," and that the "opinion reflects a reliable application of the principles and methods to the facts of the case." *Id.* at 702(b)-(d).

The admissibility of expert opinions and testimony follows the law of the regional circuit. *See Micro Chem., Inc. v. Lextron, Inc.*, 317 F.3d 1387, 1390-91 (Fed. Cir. 2003). In the Third Circuit, admissibility focuses on the "trilogy of restrictions on expert testimony: qualification, reliability and fit." *Calhoun v. Yamaha Motor Corp.*, 350 F.3d 316, 321 (3d Cir. 2003). To meet

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the fitness requirement, "the expert's testimony must be relevant for the purposes of the case and must assist the trier of fact." *Id.*

Expert opinions and testimony applying an incorrect claim construction or wrong legal standard should be excluded. *EMC Corp. v. Pure Storage, Inc.,* 154 F. Supp. 3d 81, 110 (D. Del. 2016) (excluding opinions and testimony contrary to the court's construction); *Exela Pharma Scis., LLC v. Eton Pharms., Inc.*, C.A. No. 20-CV-365 (MN), 2022 WL 806524, at *3 (D. Del. Feb. 8, 2022) (excluding opinions and testimony that "depend[] on an incorrect legal theory" or are "premised on a misunderstanding of the law").

IV. ***MOTION #1*: EXCLUSION OF NS'S EXPERT OPINIONS AND TESTIMONY APPLYING A NEW AND IMPROPER CONSTRUCTION OF "MORPHOLINO"**

A. Introduction

Despite the Court's narrowing of the claim construction, NS again asserts invalidity alleging the Asserted Claim of the '851 Patent is overbroad. Now, instead of focusing on ASOs with non-complementary bases, NS reads the claims broadly by offering a new and contradictory construction of the "morpholino" chemical backbone of the ASOs. This new construction directly contradicts sworn testimony applying the term's plain and ordinary meaning previously offered by NS's own experts, Drs. Hastings and Wood, and as used in the intrinsic record.

Having offered and accepted the narrower, correct construction of morpholino ASO during claim construction, NS cannot change course now and offer a new construction. Drs. Hastings and Wood's opinions and testimony that apply this new, incorrect "morpholino ASO" construction are inadmissible. FED. R. EVID. 702; *see, e.g., EMC Corp.*, 154 F. Supp. 3d at 109-10.

B. Argument

Drs. Hastings and Wood have each offered sworn statements acknowledging that "morpholino ASOs" have morpholino groups with phosphorodiamidate linkages. Ex. 1 (2014

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Wood Decl.) ¶¶ 52, 55; D.I. 171 at Ex. 43 ¶ 111 (which includes the below chemical structure from Summerton 1997 (Ex. 2) (color annotations added)).

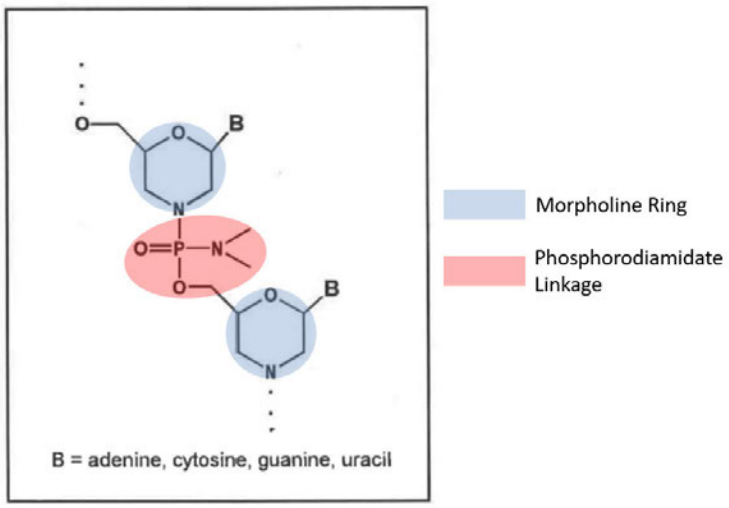

FIG. 2. Morpholino oligo structure.

Abandoning their prior position, Drs. Hastings and Wood now opine that the '851 Patent's claimed "morpholino ASOs" encompass non-phosphorodiamidate linkages.

During the original claim construction proceedings, and prior to the Court's clarification that the '851 Patent "requires 100% complementarity," Drs. Hastings and Wood applied the plain and ordinary meaning of "morpholino ASO" as having only phosphorodiamidate linkages, referred to as "Phosphorodiamidate Morpholino Oligomers" or "PMOs." Dr. Hastings's claim construction declaration expressly equated PMOs with morpholino ASOs, stating "a POSA would understand that ***PMO or morpholino oligonucleotides*** could also include a mixture of both thymine and uracil bases." D.I. 171 at Ex. 43 ¶ 110. Further, Dr. Hastings described "the design and preparation of morpholinos," specifically referencing a "structure of morpholino oligomers" figure that showed only phosphorodiamidate-linked morpholine rings. *Id*. at Ex. 43 ¶ 111 (citing Summerton 1997 at Fig. 2 (Ex. 2) (reproduced with annotations above)); Ex. 3 (Hastings Supp. Tr.) at 73:13-75:11 (confirming same). Moreover, Dr. Hastings's own ASO testing ***for this case*** aligns with her claim

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construction declaration because all the morpholino ASOs she tested used exclusively phosphorodiamidate inter-subunit linkages. Ex. 3 (Hastings Supp. Tr.) at 111:20-112:2 ("We [] tested the PMOs and the 2'-O-methyls."); Ex. 4 (Hastings Supp. Rep.) ¶¶ 163 (2'O-Me), 167 (PMOs). Dr. Hastings admitted that her tests occurred before the Court's initial claim construction order and reflected her understanding of "the breadth of the genus at that time." Ex. 3 (Hastings Supp. Tr.) at 86:3-13; *see also id.* at 82:14-83:18 ("Well, the way that . . . I was interpreting the claim when I first got involved in designing the CERI [tests]. . . I was testing sort of the breadth of the [] kind of the four corners there."). Dr. Hastings thus interpreted the "morpholino ASO" term as only using phosphorodiamidate linkages. Stated plainly, Dr. Hastings's tests reveal her objective, unfettered understanding of what linkages "morpholino ASOs" use: only phosphorodiamidates.

Likewise, Dr. Wood's 2014 Patent Office declaration stated that the term "morpholino ASOs" refers to PMOs. While describing "a selection of significant type of [ASO] chemistries proposed for exon skipping," Dr. Wood twice equated morpholino ASOs with PMOs. Ex. 1 (2014 Wood Decl.) ¶ 52 (including figure describing "Morpholino (PMO)"), ¶ 55 (phosphorodiamidate morpholino oligomers are "called 'morpholinos' or 'PMOs'"); *see also* Ex. 5 (Wood Supp. Tr.) at 117:2-119:6 (testifying that he stands by his declaration submitted to the US Patent Office in 2014 that opined "phosphorodiamidate morpholino oligomers [are] called morpholinos or PMOs") (internal quotations omitted). Even Dr. Wood's supplemental opinions and testimony in this case concede that "the term 'morpholino' is often used interchangeably with PMO." Ex. 6 (Wood Supp. Reply Rep.) ¶ 60; *see also* Ex. 7 (Wood Supp. Rep.) ¶ 82 (admitting that the "term 'morpholino is

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often used ***interchangeably*** with 'PMO'").[2]

Now that the Court's clarification requiring "100% complementarity" has significantly narrowed the Asserted Claim, NS and Drs. Hastings and Wood seek to supplant the plain and ordinary meaning of "morpholino ASO" with a new, specialized construction designed to inject breadth into the claims by permitting linkages beyond phosphorodiamidates. *See* Ex. 4 (Hastings Supp. Rep.) ¶ 61 ("I agree with Dr. Wood's conclusion that the term 'morpholino' is broader than just a ***phosphorodiamidate*** morpholino oligomer ("PMO") and encompasses ASOs with different types of morpholino intersubunit linkages."); Ex. 6 (Wood Supp. Reply Rep.) ¶ 60 ("Although the term 'morpholino' is often used interchangeably with PMO, there are examples in the contemporaneous literature where it is not.").

The Court's revised construction provides no basis for Drs. Hastings and Wood to change their definition of "morpholino ASO." *See* D.I. 573. Indeed, Drs. Hastings and Wood do not even attempt to relate the Court's revised construction to their new-found understanding of the term. No such relationship exists.

Additionally, the prosecution histories of the '851 Patent Family confirm that Drs. Hastings and Wood correctly applied the plain and ordinary meaning of "morpholino ASO" in their prior opinions. While the '851 Patent's claims and specification provide no special definition for "morpholino ASO," file history statements confirm that its plain and ordinary meaning refers to

[2] Although Dr. Wood inaptly discusses references to support his opinion that "morpholino" potentially refers to linkages other than phosphorodiamidates, the contemporaneous references he cites indicate that phosphorodiamidate-linked morpholinos were the focus for a number of reasons. *Compare* Ex. 6 (Wood Supp. Reply Rep.) ¶ 60 *and* Ex. 7 (Wood Supp. Rep.) ¶ 82 *with* Ex. 8 (U.S. Patent. No. 6,784,291) at Abstract (stating that "phosphorodiamidate-linked morpholino oligonucleotide[s]" were preferred); Ex. 2 (Summerton 1997) at SRPT-VYDS-0229439 (stating that phosphorodiamidate linkages depicted in Fig. 2 were the focus); Ex. 5 (Wood Supp. Tr.) at 124:3-11 (agreeing that Summerton 1997 focused on "phosphorodiamidate [linkages]").

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PMOs. Ex. 9 (U.S. Patent No. 9,994,851) at Cl. 1-2. For example, during prosecution of a related patent (U.S. Patent No. 9,024,007) that claims priority to the same PCT application as the '851 Patent, the applicant responded to an office action explaining that "the term 'morpholino antisense oligonucleotide' refers to the chemical structure of the oligonucleotide backbone in which six-membered morpholine rings replace ribose and nucleotides are joined by ***phosphorodiamidate linkages***." Ex. 10 (U.S. Patent No. 9,024,007 File History) at SRPT-VYDS-0247403. Additionally, the applicant noted that the term was described in the prior art, citing Summerton 1997, Heasman 2002, and Gebski 2003.[3] *Id.* at SRPT-VYDS-0247384; *see also* Ex. 12 (Dowdy Supp. Reb. Rep.) ¶ 23 (providing a table of these references). These cited references each used "morpholino ASO" to refer to a PMO. Summerton 1997—which Dr. Hastings's claim construction declaration expressly discusses—depicts the "[m]orpholino oligo structure" with phosphorodiamidate-linked morpholine rings. Ex. 2 (Summerton 1997) at SRPT-VYDS-0229438 (Fig. 2); *see also* D.I. 171 at Ex. 43 ¶ 111 (quoting same and depicting Fig. 2). Likewise, Heasman 2002 notes that "[m]orpholino oligos were designed specifically to overcome many of the limitations of regular DNA oligos (GeneTools, LLC)." Ex. 13 (Heasman 2002) at SRTP-VYDS-0247377. Heasman 2002 continues, stating that morpholinos "ha[v]e the riboside moiety of each subunit converted to a morpholine moiety (morpholine = C_4H_9NO), and uses a phosphorodiamidate intersubunit linkage instead of phosphorodiester linkages (see Summerton and Weller, 1997 for a detailed description)." *Id.* And Gebski 2003 references the ASOs discussed by Summerton 1997, reporting that "[a] chemistry that is gaining wide recognition for use in antisense applications is the morpholino . . . ." Ex. 14 (Gebski 2003) at SRPT-VYDS-0227841.

[3] Another pre-2005 reference, Aartsma-Rus 2004, equates the terms "morpholino" and "[m]orpholino-phosphordiamidate DNA." Ex. 11 (Aartsma-Rus 2004) at NS000157156.

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During prosecution of the '851 Patent itself, the applicant made similar statements and cited ***the very same references*** to explain the meaning of "morpholino ASO." Ex. 15 (Excerpt of '851 Patent Pros. History) at SRPT-VYDS-0003101. At bottom, these statements—and the literature cited to and accepted by the Patent Office—confirms that a POSA would understand "morpholino" to refer to PMOs, consistent with this term's customary usages in June 2005.

Drs. Hastings and Wood's supplemental opinions and testimony that are based on their new, contradictory construction of "morpholino ASO" are irrelevant, unreliable, and risk juror confusion because they apply an incorrect construction of the term. As such, they are inadmissible under Rule 702. Experts may not testify on claim construction to the jury. *CytoLogix Corp. v. Ventana Med. Sys., Inc.*, 424 F.3d 1168, 1172 (Fed. Cir. 2005) (ruling that expert testimony regarding claim construction was improper despite party agreement due to a "high" risk of juror confusion). And courts routinely exclude expert testimony that applies faulty claim constructions. *See, e.g., Finjan, Inc. v. Secure Computing Corp.*, 626 F.3d 1197, 1207 (Fed. Cir. 2010) (finding no error where a district court excluded expert opinions and testimony that applied a claim construction rejected by the court); *EMC Corp.,* 154 F. Supp. at 109-10 (granting *Daubert* motion to exclude expert opinions and testimony relying on incorrect claim construction); *see also Homeland Housewares, LLC v. Whirlpool Corp.*, 865 F.3d 1372, 1378 (Fed. Cir. 2017) ("[W]e must disregard the testimony of an expert that is . . . based on an incorrect understanding of the claims.") (internal quotations and alterations omitted).

This authority compels the same result here. Drs. Hastings and Wood abandoned their prior, correct understanding of "morpholino ASO" in a belated attempt to salvage NS's written description and enablement contentions. The Court should preclude NS from offering self-contradicting expert opinions and testimony that are wrong on the merits.

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V. ***MOTION #2*: EXCLUSION OF DR. WOOD'S IRRELEVANT AND UNHELPFUL OPINIONS AND TESTIMONY**

Dr. Wood's proposed opinions and testimony that are the subject of this Motion (as specified in Sarepta/UWA's *Daubert* Motion # 2) will not "help the trier of fact to understand the evidence or to determine a fact in issue" and should be excluded under Federal Rule of Evidence 702. Also, any probative value it may have is substantially outweighed by the danger of it "confusing the issues, misleading the jury, . . . or needlessly presenting cumulative evidence" and should be excluded under both Federal Rules of Evidence 403 and 702.[4] *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 746-47 (3d Cir. 1994) ("under Rule 702, admissibility of scientific testimony turns not only on reliability but also on the possibility that admitting the evidence would overwhelm, confuse, or mislead the jury" and noting that the Supreme Court's *Daubert* decision supported "application of essentially similar analysis under the rubric of Rule 403"); *Allscripts Healthcare, LLC v. Andor Health LLC*, C.A. No. 21-704-MAK, 2022 WL 3021560, at *2 (D. Del. July 29, 2022) (ruling on *Daubert* motions, explaining "Rule 702's trilogy of restrictions incorporates to some extent a consideration of the dangers, particularly the danger of unfair prejudice, enumerated in Rule 403. But Rule 403 still independently applies to expert testimony.") (internal quotation and citations omitted).

Dr. Wood—by his own admission—does not "have a direct or indirect opinion on the validity of the ['851] patent," "ha[s]n't considered" validity, and is not offering any opinions on

[4] Dr. Wood's opinions and testimony are also irrelevant to the inequitable conduct issues that will be tried to the bench and should also be excluded under Rule 702. *UGI Sunbury LLC v. A Permanent Easement for 1.7575 Acres*, 949 F.3d 825, 832 (3d Cir. 2020) ("Rule 702 applies whether the trier of fact is a judge or a jury."). Given the Court's prior ruling declining to exclude expert opinions and testimony from the bench trial in favor of conditionally admitting it subject to a later Rule 702 determination (D.I. 545 at 2-3), Sarepta's brief focuses on the issues to be tried to the jury. Sarepta will renew and further brief its Rule 702 challenge to Dr. Wood's bench-trial opinions and testimony at the Court's preferred time.

written description or enablement. Ex. 5 (Wood Supp. Tr.) at 31:10-33:21. Given that invalidity is the ***only*** issue for the jury trial on the '851 Patent that Dr. Wood's proffered opinions and testimony could be related to, they should be excluded. Consistent with his admissions, Dr. Wood submitted a sworn declaration (to overcome Sarepta's motions to exclude and strike his opinions (D.I. 308-09; D.I. 387)) that he "will not be offering opinions concerning the infringement or validity of U.S. Patent Nos. 9, 994,851" (D.I. 326 at ¶ 3), which he is "not going back on" (Ex. 5 (Wood Supp. Tr.) at 33:6-21). *See also id*. (Wood Supp. Tr.) at 32:18-33:5 ("Q. You're not providing opinions to support NS's arguments on invalidity but just not saying the words 'invalidity' yourself? . . . A. Well, I'm not expressing an opinion on the validity of the patent"). Dr. Wood also does not apply any legal standard relevant to the validity issues in the jury trial in any of his reports—not even a legal standard that defines what the scope of the prior art is or the legally relevant time point is for assessing the state of the art. The only legal standards in any of Dr. Wood's reports relate to the definition of a POSA and inventorship, which are either not disputed (POSA definition) or not relevant to ***any*** issue at trial (inventorship). Ex. 16 (Wood Open. Rep.) ¶¶ 14-16; D.I. 536 at ¶ 64 & D.I. 536-6 (showing NS does not intend to try inventorship).

Dr. Wood's proffered opinions and testimony relating to inventorship are irrelevant to the written description and enablement issues in the jury trial and do not meet the "fit" requirement for permissible expert opinions and testimony under Rule 702. Ex. 7 (Wood Supp. Rep.) ¶¶ 58, 61-76; Ex. 6 (Wood Supp. Reply Rep.) ¶¶ 11, 21-22, 27, 30, 32-33, 35-36. *Calhoun*, 350 F.3d at 321; *UGI Sunbury*, 949 F.3d at 835 ("To determine whether an expert's testimony 'fits' the proceedings, this Court asks whether it 'will help the trier of fact to understand the evidence or to determine a fact in issue.") (quoting FED. R. EVID. 702(a)). As the jury will not be tasked with determining any fact relating to inventorship when assessing written description and enablement,

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Dr. Wood's inventorship opinions and testimony are irrelevant. Worse, Dr. Wood's opinions and testimony applying the inventorship standard would overwhelm, confuse, or mislead the jury, which will be tasked with applying different legal standards for written description and enablement, violating Rules 702 and 403. *In re Paoli R.R.*, 35 F.3d at 746-47.

Dr. Wood's opinions on inventorship will be particularly confusing to the jury, given that the terms he uses in his analysis are confusingly similar to terms in the legal standard for written description, despite there being important substantive differences between those standards. Dr. Wood applies an inventorship standard that "the inventor must contemporaneously ***recognize and appreciate*** the invention, and the invention must have known utility for there to be invention." Ex. 16 (Wood Open. Rep.) ¶ 16. Throughout his supplemental expert reports, Dr. Wood opines on what Drs. Wilton and Fletcher, inventors of the '851 patent, and others "recognized and appreciated" about the invention. *See, e.g.,* Ex. 7 (Wood Supp. Rep.) ¶¶ 58, 62-63, 70-71, 73, 76; Ex. 6 (Wood Supp. Reply Rep.) ¶¶ 11, 21-22, 27, 30, 32-33, 35-36. Dr. Wood admitted that his opinions and testimony as to what Drs. Wilton and Fletcher "neither recognized nor appreciated" was "more likely [] legal terminology that was drafted for this case," was "certainly legal terminology," and was "a legal phrase [he] use[s] for purposes of [his] analysis in this case, not something that [he] typically use[s] in [his] scientific publications." Ex. 5 (Wood Supp. Tr.) at 38:15-40:23. In essence, Dr. Wood is opining on what the inventors ***subjectively knew*** about their invention applying a legal standard not used in his scientific work, rather than offering testimony about the state of the art or what the research field thought about the inventors' work at the time. Based on this analysis, Dr. Wood ultimately opines that "after reviewing the ['851 Patent's] specification, a POSA would not have understood the inventors to have possessed or invented any ***morpholino*** AONs that they knew or reasonably expected would induce exon 53 skipping." Ex. 6

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(Wood Supp. Reply Rep.) ¶ 82 (underlining added, bold italics in original). But this sounds remarkably similar to the legal standard for written description that the jury will be tasked with applying (and which Dr. Wood did not), which is an ***objective*** analysis of "whether the disclosure of the application relied upon reasonably conveys to those skilled in the art ***that the inventor had possession of the claimed subject matter*** as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). Dr. Wood testifying about his ***subjective*** inventorship analysis using terms similar to the legal standard for the ***objective*** written description standard guarantees confusing the issues and misleading the jury. Coupled with the lack of any probative value for any issue in the case, Dr. Wood's opinions and testimony concerning inventorship should be excluded under Rules 702 and 403.

To the extent NS argues that Dr. Wood's opinions and testimony are proffered to fill gaps in Dr. Hastings's written description and enablement analyses or otherwise support Dr. Hastings's opinions and testimony, that fails. Dr. Hastings testified that she did not rely on Dr. Wood's opinions but merely referred to and agreed with them, explaining "we have similar expertise in terms of use of the antisense oligonucleotides. And he agreed with me and I agreed with him on our – on our opinions." Ex. 3 (Hastings Supp. Tr.) at 14:3-15:15. As Dr. Hastings's admission makes clear, Dr. Wood's opinions and testimony—even if he had not applied an irrelevant and confusing legal standard—would be needlessly cumulative to and improperly bolstering of Dr. Hastings's proposed opinions and testimony.[5] "The general rule of thumb, in this District at least, is that a party is not allowed to present more than one expert to say the same thing." *Reckitt Benckiser Pharms. Inc. v. Watson Lab'ys, Inc.*, C.A. No. 13-674-RGA, 2015 WL 6456551, at *1

[5] Avoiding needlessly cumulative testimony is important here, where the Court has allowed only 11 hours to each side to present their case to the jury, including openings and closings (D.I. 536 at ¶ 75), and NS intends to present 24 witnesses live or by deposition (D.I. 536-11 at 2-3).

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& n.1 (D. Del. Oct. 26, 2015). Courts in this district have also excluded opinions and testimony that merely agrees with another expert or "serves no purpose beyond improperly attempting to bolster the opinions of another expert." *Roche Diagnostics Corp. v. Meso Scale Diagnostics, L.L.C.*, C.A. No. 17-189-LPS-CJB, 2019 WL 5310220, at *3 (D. Del. Oct. 21, 2019). As Dr. Hastings admitted, Dr. Wood's proposed opinions and testimony do both. The Court should exclude Dr. Wood's opinions and testimony entirely.

VI. ***MOTION #3*: EXCLUSION OF DR. HASTINGS'S OPINIONS AND TESTIMONY CONCERNING ENABLEMENT OF 5'- AND 3'-END MODIFICATIONS**

NS's expert, Dr. Hastings, should also be precluded from telling the jury that Sarepta's '851 Patent does not enable "5'- and 3'-end modifications" (*i.e.*, conjugating distinct chemical groups to the ends of the ASOs recited in Claim 1). It is undisputed that the claim does not recite any such modifications. To be sure, such modifications are ***not excluded*** from the claim; the preamble of the claim uses the term "comprising," which is ubiquitous in patent claims and allows for additional unrecited elements, including end modifications. But, as a matter of law, a patent must only enable the invention as recited in the claims, not every conceivable unrecited element that could be used with the claimed invention.[6] Because Dr. Hastings misapplies the enablement standard, her opinions and testimony are unreliable and will not be helpful to the jury and should be excluded. FED. R. EVID. 702; *Inline Connection Corp. v. AOL Time Warner Inc.*, C.A. No. 02-272-MPT, 2007 WL 275928, at *5 (D. Del. Jan. 29, 2007) ("Because [the expert] did not conduct

[6] *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1371 (Fed. Cir. 2023), *cert. denied*, 144 S. Ct. 873 (2024) ("Again, because safety and efficacy are not recited in the claims, we need not deal with Liquidia's [enablement and written description] arguments."); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1557 (Fed. Cir. 1983) ("Calculation of minimum stretch rate above 35°C is nowhere in the claims."); *Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F. Supp. 1278, 1292 (D. Del. 1987), *aff'd*, 865 F.2d 1247 (Fed. Cir. 1989) ("The applicant is not required to include in his application support for matters not set forth in the claim. As explained supra, there is no limitation in the '851 claim regarding intrinsic viscosity or molecular weight.").

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a proper enablement analysis, his opinion is not reliable and is not admissible on enablement. As a result, [the expert's] opinion and testimony regarding enablement is excluded.").

Claim 1 of the '851 Patent recites a narrowly-tailored genus of ASOs; the claim includes structural elements—none of which are 5'- or 3'-end modifications.[7] *See* Ex. 3 (Hastings Supp. Tr.) at 79:5-15 ("[T]he claim doesn't talk about what the end is."), 60:6-22 ("[I]t doesn't talk about the other modifications . . ."). Dr. Hastings misapplies enablement law by opining that the '851 Patent fails to enable 5'- and 3'-end modifications that are nowhere in the claim.[8]

The Federal Circuit has repeatedly held that a patent need not enable unrecited claim elements. As recently as this year, the Federal Circuit was faced with this issue in the context of claims directed to "a method of treating pulmonary hypertension comprising inhalation of treprostinil." *United Therapeutics*, 74 F.4th at 1364. The claims did not recite safety or efficacy

[7] Claim 1 of the '851 Patent recites: "An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69), wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof."

[8] *See, e.g.,* Ex. 4 (Hastings Supp. Rep.) ¶ 55 ("According to the ['851 Patent] specification, '[a]nother modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates.' . . . [T]hese classes involve modifying ASOs by performing a chemical modification at either the 5' or 3' (or both) ends of the antisense oligonucleotides . . ."); ¶ 75 ("To estimate the 'full scope' of ASOs meeting the claims' structural limitations and not just the 'target regions'—a POSA would first consider the chemical variabilities taught by the specification to be possible. As discussed above, supra Section VIII.B, the specification describes . . . at least nineteen different options for chemical moieties."), ¶ 207 ("Making the 'full scope' would require evaluating—at the specification's urging—. . . chemical moieties with morpholino ASOs for which there was no guidance."); ¶ 209 ("Given the limited commercial availability of only certain PMOs at the time, the chemical synthesis efforts required to be able to make the full scope of the genus (e.g., 31mers, ASOs with chemical moieties . . .) would itself be undue."); *see also id.* ¶¶ 56-60, 65, 76, 79, 81; Ex. 17 (Hastings Supp. Reply) ¶¶ 91, 93, 96, 99, 117.

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limitations (though the claimed method plainly permitted both). *Id*. at 1369. As a result, the Federal Circuit rejected defendant's argument that the patent at issue had to enable safe and effective treatment in every patient subpopulation. *Id*. at 1370-71.

Similarly, in *W.L. Gore*, the claims at issue were directed to "processes for stretching" PTFE (aka Teflon®) tape; the processes included "stretching PTFE at a rate above 10% per second and at a temperature between about 35°C and the crystalline melt point of PTFE." 721 F.2d at 1545. The defendant argued that the claims were not enabled because "the minimum rate of stretch may increase with temperature," and yet the patent did not disclose "a method for calculating the minimum rate of stretch above 35°C." *Id*. at 1557. As in *United Therapeutics*, the claims in *W.L. Gore* allowed for unrecited elements; the claimed processes in *W.L. Gore* covered processes that adjusted the stretching rate based on temperature. The Federal Circuit again rejected the non-enablement argument because it was not directed at any element recited in the claims: "Calculation of minimum stretch rate above 35°C is nowhere in the claims, and it is the *claimed* invention for which enablement is required." *Id*. (emphasis in original).

Delaware courts have followed suit. In *Phillips*, the court held that the patent did not need to enable polypropylene with high-viscosity, because that property was not recited in the claims:

> Defendants have again missed the point of the inquiry under section 112. As the Federal Circuit has explained, it is the *claimed* invention for which enablement is required. *W.L. Gore*, 721 F.2d at 1557; *see also DeGeorge*, 768 F.2d at 1323. ***The applicant is not required to include in his application support for matters not set forth in the claim***. *DeGeorge*, 768 F.2d at 1324. As explained *supra*, there is no limitation in the '851 claim regarding intrinsic viscosity or molecular weight. Even assuming arguendo that the [earlier] application did not enable one skilled in the art to produce polypropylene having an intrinsic viscosity greater than 1.0, Phillips' disclosure would not be rendered non-enabling.

Id. (regular italics in original; bold italics added).

Dr. Hastings makes precisely the same erroneous enablement argument that the Federal Circuit has rejected time and again. Such unreliable and unhelpful opinions and testimony should

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be excluded.

VII. *MOTION #4*: EXCLUSION OF DR. HASTINGS'S OPINIONS AND TESTIMONY APPLYING INCORRECT WRITTEN DESCRIPTION LAW

Dr. Hastings's supplemental reports include proposed opinions and testimony that depend on an incorrect application of written description law. As such, they are unhelpful to the trier of fact and should be excluded under Rule 702. Indeed, "courts routinely preclude those portions of an expert's report that are premised on a misunderstanding of the law." *Exela Pharma Scis.,* 2022 WL 806524, at *3 (collecting cases). The portions of Dr. Hastings's reports discussed below that are premised on a misunderstanding of written description law should likewise be excluded.

A. Dr. Hastings's Opinions and Testimony Are Not an Objective Inquiry into the Four Corners of the Specification and Should Be Excluded

As Dr. Hastings acknowledges, the law requires that written description be analyzed by assessing the disclosure within the four corners of a patent. Ex. 4 (Hastings Supp. Rep.) ¶ 134 ("Although I understand that the written description is judged from the disclosure within the four corners of the patent disclosure, I nevertheless looked at [redacted]"). But she "nevertheless" goes on to assess materials beyond the '851 Patent to "support" her written description arguments. She even admits in her own words that her analysis is "subjective," not objective. Ex. 3 (Hastings Supp. Tr.) at 39:13-41:20. Reliance on such extraneous materials is premised on the incorrect legal theory and a misunderstanding of written description law that it is permissible to do so. It is not, and Dr. Hastings's opinions and testimony on this point should be excluded. Ex. 4 (Hastings Supp. Rep.) ¶¶ 110 & n.16, 128-132, 134-153; Ex. 17 (Hastings Supp. Reply Rep.)¶¶ 65-67, 75, 81 & n.20, 86.

Dr. Hastings's opinions and testimony are based largely on extrinsic evidence outside of the four corners of the patent—including an entire section titled "My Review of [redacted] Supports My Opinions . . .". Ex. 4 (Hastings Supp. Rep.) ¶¶ 134-153.

[redacted]

Throughout both of her reports (Ex. 4 (Hastings Supp. Rep.) ¶¶ 128-132 & n.18, 134-153; Ex. 17 (Hastings Supp. Reply Rep.) ¶¶ 65-67, 75, 81 & n.20, 86), Dr. Hastings relies on [redacted] to argue that the '851 Patent lacks written description. That is, instead of looking to the specification, which on its face provides specific examples of ASOs within the hotspot that demonstrate skipping (Ex. 9 ('851 Patent) at Table 39), Dr. Hastings looks to unincorporated extrinsic evidence to determine that she was [redacted] to support her subjective claim that the data is [redacted] Ex. 4 (Hastings Supp. Rep.) ¶ 142.

This analysis runs afoul of the Federal Circuit's guidance for written description analysis, which "requires an ***objective*** inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art" to determine whether there is "possession as shown in the disclosure." *Ariad Pharms.,* 598 F.3d at 1351 (rejecting a view of "possession" that looks to whether the inventor "can produce records documenting" the work). While expert opinions and testimony are permissible for written description, "proper inquiry must be into the specification first and then *guided* by expert testimony." *Allergan USA, Inc. v. MSN Lab'ys Priv. Ltd.*, 111 F.4th 1358, 1376 (Fed. Cir. 2024) (emphasis in original). Expert opinions and testimony that are not tethered to "*some* basis in the specification" are not permissible, as "untethered to the inventors' own description of the invention, [they] would improperly take the written description inquiry outside the four corners of the specification." *Id.* (emphasis in original). Dr. Hastings's analysis does just that. Dr. Hastings could—and should—have objectively analyzed the specification from the perspective of a POSA to determine if it ***disclosed*** the invention. Instead, she inappropriately sought the information elsewhere, outside of the four corners of the specification, to back up her subjective doubts regarding the data presented in Table 39. But such doubts are not relevant to the

written description analysis.

Instead of looking objectively at the disclosures within the four corners of the '851 Patent, Dr. Hastings subjectively casts doubt on the data reported in the specification, resorting to outside evidence to attempt to manufacture a shortcoming where none exists. A proper analysis would look to the disclosure of the specification, which fully supports the written description of the '851 Patent. *Ariad*, 598 F.3d at 1351. Dr. Hastings's opinions and testimony regarding extrinsic evidence are therefore irrelevant and based on an improper understanding of the law. Paragraphs 110 & n.16, 128-132, and 134-153 of Dr. Hastings's Supplemental Opening Expert Report and paragraphs 65-67, 75, 81 & n.20, and 86 of Dr. Hastings's Supplemental Reply Expert Report should be excluded.

B. Dr. Hastings's Opinions and Testimony Requiring Proof of Therapeutic Efficacy and Evidence of Exon Skipping Should Be Excluded

Dr. Hastings also applies a heightened, improper standard of proof to the data and information disclosed in the '851 Patent. Specifically, Dr. Hastings faults the '851 Patent for not including data showing ASOs that have a "therapeutic effect" or "therapeutic levels" of exon skipping. Ex. 4 (Hastings Supp. Rep.) ¶¶ 109-110, 112; Ex. 17 (Hastings Supp. Reply Rep.) ¶ 81; Ex. 3 (Hastings Supp. Tr.) at 35:4-36:13, 40:6-41:9, 41:11-20, 47:8-19, 48:17-49:5. Dr. Hastings bases her opinion on her understanding that sufficient written description requires both description of the invention ***and*** evidence to demonstrate that exon skipping is induced. *See, e.g.,* Ex. 3 (Hastings Supp. Tr.) at 40:22-41:20. Such considerations go well beyond the legal standard for written description, which requires only that "a claimed invention need successfully operate only to some limited degree. It need not be the best or the only way to accomplish a certain result, and it need only be useful to some extent and in certain applications." *Allergan USA*, 111 F.4th at 1376 (internal quotations omitted); *see also Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1191

[redacted]

(Fed. Cir. 2014) (explaining written description "is not about whether the patentee has proven to the skilled reader that the invention works").

First, the Asserted Claim does not recite a requirement that ASOs induce ***therapeutic levels*** of exon skipping. Rather, the Asserted Claim recites "wherein the antisense oligonucleotide induces exon 53 skipping." Ex. 9 ('851 Patent) claim 1. Although ASOs that induce therapeutic levels of exon skipping are included in the claim, for written description purposes, all that need be shown is that the '851 Patent discloses ASOs that induce some level of exon skipping. *See In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995) (rejecting argument that human clinical trials are necessary to be "useful" under Section 112, stating "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans."). This standard is met. As Dr. Hastings (begrudgingly) admits, the '851 Patent "said that there was going to be skipping" for an ASO with a sequence (+23+47) that falls within the Asserted Claim. Ex. 3 (Hastings Supp. Tr.) at 38:23-41:20; *see also id.* at 37:9-38:7 (agreeing "[t]hat's what it says, yes" when asked "according to the patent, it reports very faint skipping, correct?"). And Dr. Hastings admits that when she made and tested an ASO with that sequence attempting to reproduce the conditions in the '851 Patent, she "did see skipping." Ex. 3 (Hastings Supp. Tr.) at 38:23-41:20. Dr. Hastings's written description opinions and testimony that are premised on her misunderstanding of written description law as requiring disclosure of induction of therapeutic levels of exon skipping should thus be excluded. Ex. 4 (Hastings Supp. Rep.) ¶¶ 109, 110; Ex. 17 (Hastings Supp. Reply Rep.) ¶ 81.

Second, Dr. Hastings's written description opinions that the '851 Patent has to both describe ASOs that induce exon skipping ***and provide evidence of such skipping*** is also premised

[redacted]

on a misunderstanding of written description law. *See, e.g.,* Ex. 3 (Hastings Supp. Tr.) at 40:22-41:20 (explaining her understanding that, for the written description requirement to be met, the patent "has to describe it ***and it has to demonstrate that there is exon 53 skipping***. I don't know about – it has to skip – it has to skip. And this one, ***I did not see that there was evidence. I mean, they can write what they want there.***"). "[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Ariad Pharms.,* 598 F.3d at 1352; *Alcon Rsch.*, 745 F.3d at 1191 ("[W]ritten description is about whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described; it is not about whether the patentee has proven to the skilled reader that the invention works"). Thus, even if the '851 Patent inventors had described their exon skipping data prophetically, that would be sufficient.[9] Dr. Hastings's opinions apply an incorrect legal theory because she rejects the actual words written in the '851 Patent that disclose an ASO with a sequence covered by the claims induced exon 53 skipping and finds a lack of written description because she "did not see that there was evidence." Ex. 3 (Hastings Supp. Tr.) at 40:22-41:9. As such, her opinions and testimony are premised on a misunderstanding of written description law and should be excluded.

VIII. CONCLUSION

Sarepta and UWA respectfully request that the Court exclude opinions and testimony of NS's experts as discussed herein and specified in the accompanying motions.

[9] Indeed, as Dr. Hastings's own testing recreating the conditions of the '851 Patent showed, the '851 Patent inventors' statement that the tested ASO showed exon 53 skipping is correct. Ex. 3 (Hastings Supp. Tr.) at 39:13-21.

[redacted]

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October 2, 2024

CERTIFICATE OF SERVICE

I hereby certify that on October 2, 2024, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on October 2, 2024, upon the following in the manner indicated:

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